



Recurrence Rate of Giant-Cell Tumor Treated by Curettage and Cementation

Índice de recurrencia de tumor de células gigantes con curetaje y cementación

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Abstract

Objective To identify the recurrence rate of giant-cell tumor (GCT) in patients treated by curettage and adjuvant therapy with polymethyl metacrylate with a minimum follow-up of 3 years.

Methods Observational and retrospective cohort with patients with diagnoses of Enneking stages 1 and 2 GCT treated through intralesional curettage and cementation between 1981 and 2011. Age, gender, anatomic location and relapse period were recorded. The data was analyzed with measures of central tendency and dispersion (standard deviation) for the quantitative variables, percentages for the qualitative variables.

Results Between 1981 and 2011 375 cases of GCT were identified, 141 (36.7%) of which were treated by this method. The follow-up ranged from 48 to 240 months, the age was of 27 ± 9 years, 45% of the patients were female, and 55%, male, with a female:male ratio of about 1.2:1. The tibia was the most frequent affected bone (38%), followed by the femur (32%), the humerus (16%), and the radius (10%). The resection technique was intralesional curettage in about 88.6% of the cases, and marginal resection in the remaining cases. Pathologic fracture was present in approximately 15.7%, and recurrence occurred in approximately 12.7%.

Discussion We demonstrated that this treatment method decreases the risk of recurrence due to the local adjuvant effects of acrylic cementation. Recurrence events occur in the first two years after resection. However, some authors defend that the surgical margin is the only factor that influences the risk of local recurrence. The extraosseous extension of GCT is not a contraindication to perform intralesional curettage or to prescribe the adjuvant treatment with polymethyl metacrylate.

Conclusions We reported a recurrence rate similar to that of the literature, and this is a feasible resource for limb reconstruction.

Keywords

- ▶ giant-cell tumor
- ▶ treatment
- ▶ resection
- ▶ polymethyl metacrylate

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Resumen

Objetivo Identificar la tasa de recurrencia de tumor de células gigantes (TCG) en pacientes tratados con curetaje y cementación con seguimiento mínimo de tres años.

Material y métodos Cohorte retrospectiva y observacional de pacientes con diagnóstico de TCG en estadios 1 y 2 de Enneking tratados con curetaje intralesional y cementación entre 1981 y 2011. Se registraron edad, sexo, región anatómica, y tiempo de recurrencia. Se utilizó estadística descriptiva con medidas de tendencia central y medidas de dispersión (desviación estándar) para variables cuantitativas, y porcentajes para variables cualitativas.

Resultados Entre 1981 y 2011, se identificaron 375 casos de TCG, de los cuales 141 (37,6%) fueron tratados con este método. El seguimiento fue de 48 a 240 meses, y la edad, de 27 ± 9 años; 45% de los pacientes eran mujeres, y 55%, varones, con una relación mujer:hombre de 1,2:1. El hueso más afectado fue la tibia (38%), seguida del fémur (32%), del húmero (16%), y del radio (10%). En 88,6%, la resección fue curetaje intralesional, y el resto, marginal. Hubo 15,7% de casos de TCG con fractura, y recidiva en 12,7%.

Discusión Se ha demostrado que este método de tratamiento reduce el riesgo de recurrencia por los efectos adyuvantes locales de la cementación acrílica. La recurrencia ocurre en los dos primeros años de seguimiento. Sin embargo, hay autores que respaldan que el margen quirúrgico es el único factor que influencia el riesgo de recurrencia local. La extensión extraósea del TCG no es contraindicación para curetaje intralesional y adyuvante con metilmetacrilato.

Conclusiones Reportamos una tasa de recurrencia similar a la de la literatura, siendo un recurso factible de reconstrucción de miembros.

Palabras clave

- ▶ tumor de células gigantes
- ▶ tratamiento
- ▶ resección
- ▶ polimetilmetacrilato

Introduction

Giant cell tumor (GCT) of the bone is a neoplasm of mesenchymal origin that commonly presents as an osteolytic lesion at the epiphysal-metaphyseal region of long bones. It accounts for more than 20% of all primary bone neoplasms and 5% of primary bone tumors in adults. It typically affects patients aged from 20 to 50 years, with no gender-related differences.^{1,2} It is locally aggressive in skeletally-mature patients in more than 80% of cases, and it occurs around the knee in 75% of patients.² The distal radius is affected in 10% of 15% of the cases,³ and this is a site particularly prone to recurrence.⁴

Local recurrence is commonly due to narrow surgical margins.³

Several modalities have been used to treat GCTs. However, recurrence rates range from 10% to 54%, reflecting therapeutic efficacy.⁵ The optimal treatment for GCTs remains controversial.⁶

The present study aims to identify the recurrence rate of CGT in patients treated with curettage and cementation during a minimum follow-up of 3 years (► **Figure 1**).

Material and Methods

Retrospective and observational cohort of a registry of patients diagnosed with GCT of any gender and age treated with intralesional curettage and cementation from 1981 to

2011. The cases eligible for this treatment were those in Enneking stages 1 and 2 (with no soft-tissue invasion). Age, gender, anatomical region, recurrence, and mean time until recurrence were identified.

The sampling technique was convenience of consecutive cases.

Descriptive statistics were used with measures of central tendency (mean, median, and mode) for non-grouped quantitative variables, in addition to dispersion measures (standard deviation). We used descriptive statistics with frequency measures, that is, percentages for qualitative variables. Incidence calculations were performed.

The present article is in accordance with the ethical standards for scientific research on human beings of the Nuremberg Declaration and its amendments. In addition, it is in full compliance with the Regulations of the Mexican General Health Law on Health Research and institutional ethical standards. Informed consent letters were not required since information was obtained from secondary sources.

The research team did not receive third party contributions or sponsorships.

Results

In total, 375 cases of GCT were reviewed. The mean age at presentation was 27 years, (mean: 27 ± 11.9 years; range: 12 to 80 years), with a peak of incidence in the third decade of



Fig. 1 Trans- and postsurgical exemplification: (A) Transoperative radiograph after intralesional curettage and preparation of the Campanacci stage-II giant-cell tumor cementing bed associated with a pathological fracture of the tibial plateau. (B) Radiograph at 15 years of follow-up with no cement loosening and 6.5-mm screws, without radiographic data indicating recurrence.

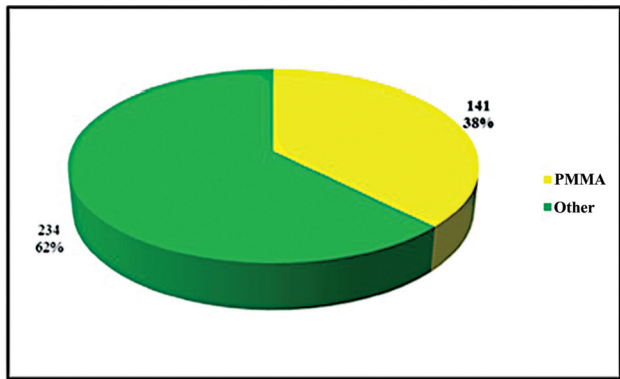


Fig. 3 Treatment modality for giant-cell tumor. PMMA (polymethyl methacrylate): Curettage and cementation. Other: other treatment modalities.

life (45.33%, $n = 233$). Regarding gender, 190 cases (50.6%) occurred in men, and 185 (49.4%), in women, with a male-to-female ratio of 1.03:1 (► **Figure 2**).

A total of 141 cases (37.6%) were treated by curettage and cementation (► **Figure 3**). The mean follow-up was of 144 months, ranging from 48 to 240 months. In subjects treated with this method, the mean age was 27 ± 9 years (range: 13 to 64 years); regarding gender, 77 (54.6%) cases occurred in men, and 64 (45.4%), in women.

All treated cases occurred in the appendicular skeleton, including 38.3% (54 cases) in the tibia, 32.6% (46 cases) in the femur, 11.3% (16 cases) in the humerus, 8.5% (12 cases) in the radius, 3.5% (5 cases) in short bones, 2.8% (4 cases) in the ulna, 1.4% (2 cases) in the clavicles, and 1.4% (2 cases) in the fibula. Pathological fracture was observed in 22 (15.7%) cases (► **Figure 4**).

Recurrence occurred in 12.7% (18) of the cases (► **Figure 5**). In total, 16 patients underwent en bloc resection as the surgical treatment, and reconstruction was carried out with resection arthrodesis with an endomedullary nail in 6

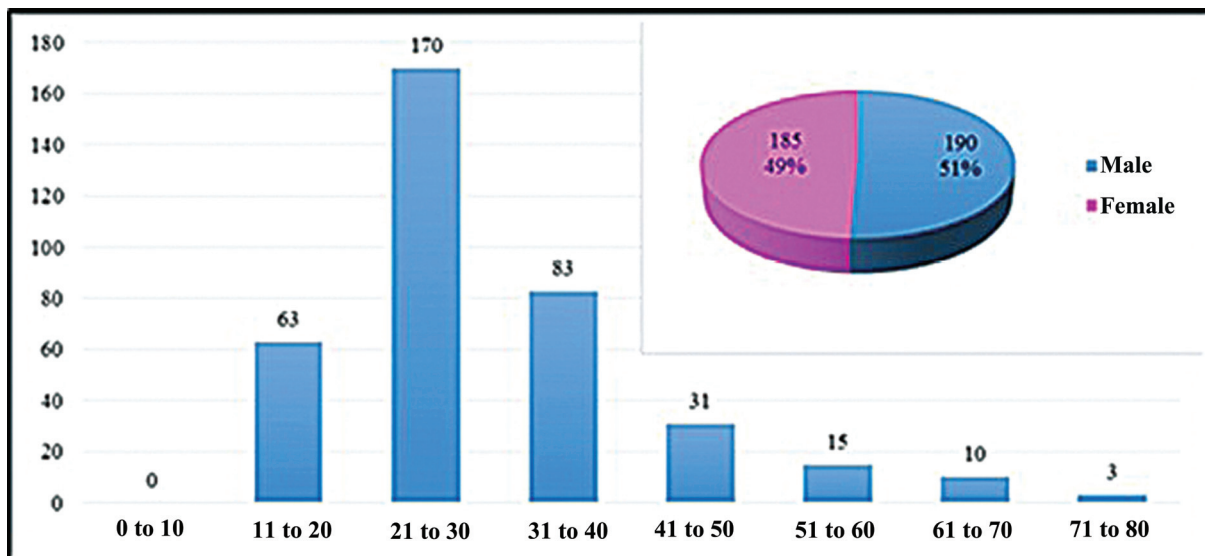


Fig. 2 Distribution of cases of giant-cell tumor regarding age and gender.

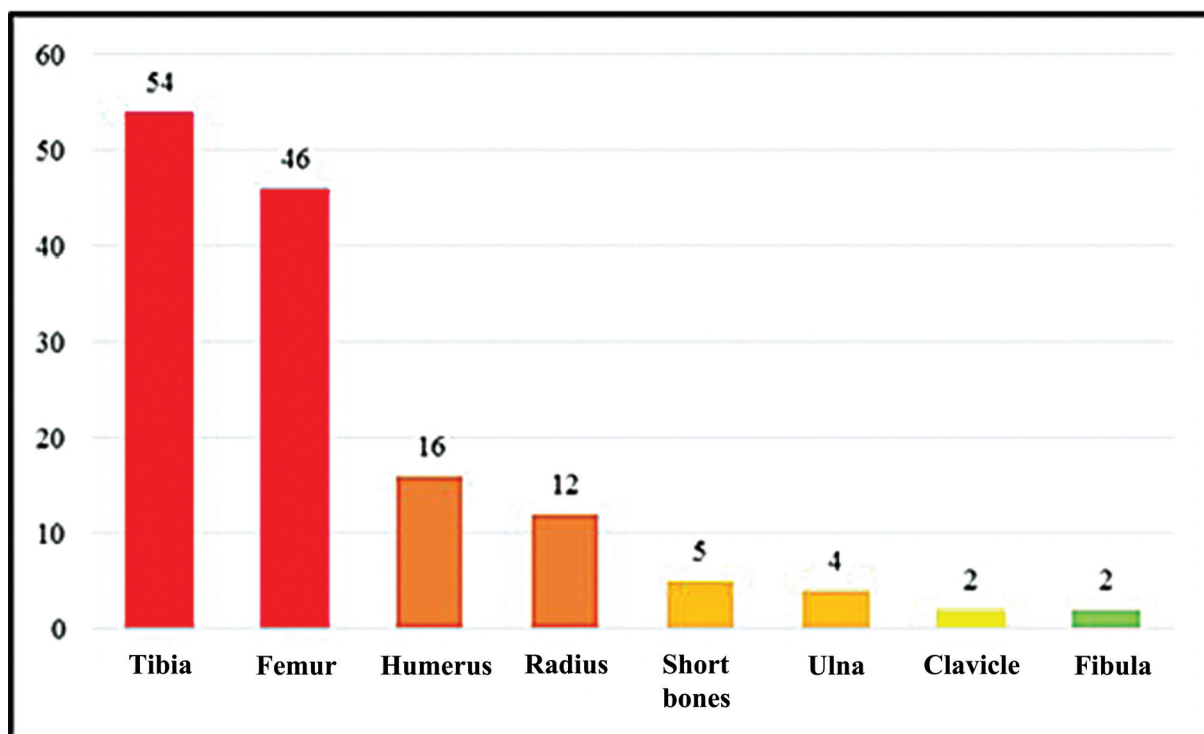


Fig. 4 Sites of anatomical involvement with giant-cell tumor treated by curettage and cementation. Note the higher number of cases in the long bones of the lower limb.

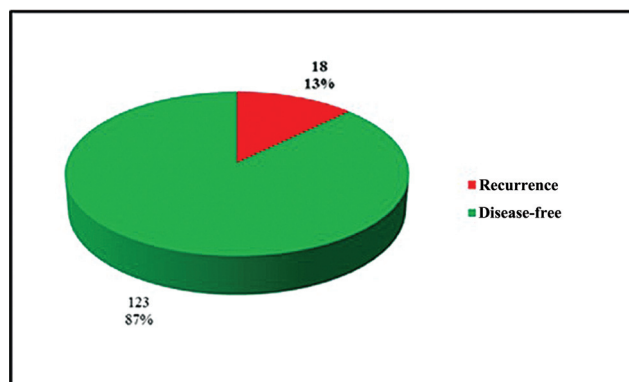


Fig. 5 Recurrence rate in giant-cell tumor treated with curettage and cementation. No case was submitted to revision curettage and

cases, tumor prosthesis in 9 cases, and external fixation in 1 case; another case underwent a new marginal resection and cementation, and 1 case was not treated due to hematological complications (*coagulopathy*).

Discussion

The classic treatment for CGTs has been curettage and bone grafting to preserve the function of the adjacent joint.⁷ In 1969, Vidal et al.⁸ treated 2 cases of GCT with acrylic cement in an attempt to create stability after surgical curettage. Persson et al.⁷ treated 14 patients using this method, with a recurrence rate of 15%. This technique is simple, with no

need for bone grafting. In addition, it provides immediate fixation and stabilization, and spares joint function. Disease control is improved, and local recurrence is easy to detect.⁵

Regarding cementation, heat treatment lowers cell viability.⁵ Wilkins et al.⁹ demonstrated bone necrosis at 60° C. Leeson¹⁰ showed that the polymerization reaction produces necrosis, extending the macroscopic surgical margin and decreasing the probability of recurrence; on the other hand, it releases a toxic monomer.¹¹ The margins obtained with this technique are between 1.5 mm to 2 mm in cancellous bone and of 0.5 mm in cortical bone.¹²

Another advantage of cementation is the possibility of immediate fixation and stabilization of large defects, especially in load-bearing bones.⁵ In contrast, if the construct fails, methyl methacrylate does not prevent other forms of treatment, such as bone grafting or total joint reconstruction.⁶

Currently, there is no consensus on the optimal curettage surgical technique, including adjuvants to limit recurrence, and possibly combined with high-speed reaming to improve the effectiveness of the curettage.^{3,13,14}

Most recurrences occur within 2 years of the initial surgery, but can be observed up to 7 years after the surgical treatment.¹³

O'Donnell et al.¹⁶ studied 69 patients and noted a local recurrence rate of 25%, with a mean time until onset of 2 years, regardless of age and gender; the recurrence rate was higher in patients not treated with high-speed ream or phenol application. For Jamshidi et al.,² recurrence occurred after a mean time of 30 months (range: 6 to 54 months), with higher rates after simple curettage (33.3%) compared to high-

speed reaming (16.6%); there were no differences regarding cementation, confirming the findings from O'Donnell et al.¹⁶ Zuo et al.³ demonstrated that this method reduces the risk of recurrence. Bini et al.⁶ observed a recurrence rate of 8% in 38 patients. In one case, recurrence was in soft tissues, while the remaining were local, suggesting that the low primary recurrence depends on meticulous and aggressive debridement and on the local adjunctive effects of acrylic cementation.⁶ Boons et al.¹² described one case of recurrence in four patients. Becker et al.¹⁴ reported a higher risk of local recurrence in extracompartmental tumors, and this method reduces the risk of local recurrence by 22% compared to simple curettage and bone graft provision. Recurrence-free outcomes were observed in 87% of intracompartmental tumors treated with this method compared to 64% of extracompartmental lesions.¹⁴ Kivioja et al.¹⁷ reported a rate of 19% of local recurrence, including 75% of cases diagnosed within the first 2 years after surgery, and none after 5 years. Gitelis et al.¹⁸ reported recurrences in 12.5% (5) of their patients during a mean follow-up of 58.2 months.¹⁸ Labs et al.¹⁹ reported a local recurrence rate of 13.3% (2 patients), with only one case treated with methyl methacrylate adjuvant. Fraquet et al.²⁰ studied 30 patients and reported a recurrence rate of 30%, including 77% within the first 2 years of follow-up, and 66% in the distal femur. According to these

authors,²⁰ the cytotoxic properties of the cement can reduce recurrence from 25% to 17%. Zhang et al.²¹ evaluated 101 patients with a recurrence of 12.7%, and concluded that the key aspect is aggressive curettage and the use of cement as an adjuvant. In 91 patients, Balke et al.²² described recurrences in 27.6% of the patients treated with this method, reducing this possibility by a factor of 8 when compared with isolated intralesional curettage. Portabella et al.²³ treated 10 cases of GCTs with curettage and cementation during a mean follow-up period up of 11 years without observing recurrences; these outcomes were attributed to the surgical technique.²⁴

In the Mexican population, Moreno-Wright et al.¹¹ found a recurrence rate of 25.7% from 6 to 16 months of follow-up, and 1 (2.8%) patient died due to tumor activity, and the remaining subjects were treated with en bloc resection.¹¹

Regarding the treatment consisting of intralesional curettage and phenol and methyl methacrylate as adjuvants.²⁵ Klenke et al.²⁶ evaluated 41 patients submitted to intralesional curettage treatment, and observed a recurrence rate of 25% and a mean interval of recurrence of 16 ± 12 months; subjects treated with local methyl methacrylate and phenol had a better recurrence-free survival rate (85%) compared to those submitted to a bone graft with the application of phenol (66%); as such, the use of phenol did not improve the recurrence-free rate.²⁶ Lackman et al.²⁷ evaluated 63

Table 1 Details from published series on giant cell tumors and cementation

| AUTHOR | YEAR | CASES | FOLLOW-UP (months) | TREATMENT | RECURRENCE |
|------------------------------------|------|-------|--------------------|------------------|------------|
| Persson et al. ⁷ | 1984 | 14 | — | MR and PMMA | 15.0% |
| Rock ³⁰ | 1990 | 677 | — | Variable | 25.5% |
| O'Donnell et al. ¹⁶ | 1994 | 69 | 48 | MR, PMMA, phenol | 25.0% |
| Bini et al. ⁶ | 1995 | 38 | 63 | MR, PMMA | 8.0% |
| Dreinhöffer et al. ³² | 1995 | 10 | — | MR, PMMA | 40.0% |
| Portabella et al. ²³ | 1998 | 10 | 132 | MR, PMMA | 0.0% |
| Zhang et al. ²¹ | 1999 | 101 | 96 | MR, PMMA | 12.7% |
| Labs et al. ¹⁹ | 2001 | 11 | 56 | MR, PMMA | 13.3% |
| Boons et al. ¹² | 2002 | 4 | 84 | MR, PMMA | 25.0% |
| Moreno-Wright et al. ¹¹ | 2003 | 31 | 56.5 | MR, PMMA | 27.5% |
| Saiz et al. ²⁸ | 2004 | 40 | — | MR, PMMA, phenol | 12.5% |
| Gitelis et al. ¹⁸ | 2005 | 40 | 58.2 | MR, PMMA | 12.5% |
| Lackman et al. ²⁷ | 2005 | 63 | 108 | MR, PMMA, phenol | 5.4%-7.7% |
| Jamshidi et al. ² | 2008 | 82 | 74 | MR, PMMA | 16.6% |
| Becker et al. ¹⁴ | 2008 | 102 | 64.2 | MR, PMMA | 22.0% |
| Kivioja et al. ¹⁷ | 2008 | 194 | 2.4-216 | MR, PMMA | 19.0% |
| Balke et al. ²² | 2008 | 91 | 12.4 | MR, PMMA | 27.6% |
| Fraquet et al. ²⁰ | 2009 | 30 | 76 | MR, PMMA | 30.0% |
| Klenke et al. ²⁶ | 2011 | 41 | 108 | MR, PMMA, phenol | 25.0% |
| Zuo et al. ^{3*} | 2013 | 374 | 60-108 | MR, PMMA | — |
| Gao et al. ²⁹ | 2014 | 31 | 38.8 | MR, PMMA | 12.9% |
| Abat et al. ²⁴ | 2015 | 71 | 144 | MR, BG | 28.2% |

Abbreviations: BG, bone graft; PMMA, polymethyl methacrylate; MR, marginal resection.

Note: *Systematic review and meta-analysis

patients, and reported a local recurrence rate ranging from 5.4% to 7.7%. Saiz et al.²⁸ evaluated 40 patients submitted to this type of treatment, and described a recurrence rate of 12.5% in a mean period of 11 months.

Gao et al.²⁹ reported local recurrence in 12.9% of the cases treated with curettage and cementation, including 81.3% within the first 2 years of follow-up.

In 677 cases treated with intralesional resection and various adjuvants, Rock³⁰ observed a total recurrence rate of 25.5% in a mean period of 21 months, including 81% of recurrences within the first 3 years of follow-up. McDonald et al.³¹ identified the surgical margin as the only factor influencing the risk of local recurrence.

Dreinhöfer et al.³² reported 10 cases of fracture upon presentation which were treated with curettage and cementation. These authors³² described a recurrence rate of 20% within the first year of follow-up, and a total recurrence rate of 40%. They recommend this method for pathological fractures.³² However, O'Donnell et al.¹⁷ reported a recurrence rate of 50% in patients with pathological fractures (–Table 1).

According to Lackman et al.,²⁷ Dreinhöfer et al.,³² and other authors, the extraosseous extension of a GCT is not a contraindication to intralesional curettage and adjuvant treatment with methylmethacrylate.^{26,32}

Using adjuvants, the recurrence rate ranges from 27% to 15% compared to 49% with isolated intralesional curettage.¹⁵ Turcotte³³ reported similar recurrence rates without methyl methacrylate or other adjuvants, contradicting this premise. However, Abat et al.²⁴ observed a recurrence rate of 28.2% in 71 cases treated with resection and bone grafting in the residual defect, with a mean follow-up time of 12 years.

Gambini et al.³⁴ reported the use of adjuvant therapy as part of the treatment for GCT. In addition, they described a lower risk of recurrence due to thorough tumor excision, since adjuvants alone cannot prevent recurrence if the tumor is not properly removed.

Some of the recommendations of surgical techniques made by other authors for GCT treatment include adequate exposure, tumor isolation, careful manipulation to avoid soft-tissue contamination, thorough curettage, intracavitary reaming, adjuvant use, and proper bone reconstruction.³⁵

Conclusion

According to the available evidence, in our environment, intracompartmental resection combined with acrylic cementation for the treatment of GCT is a viable option, with recurrence rates consistent with those reported by other authors.

Conflict of Interests

The authors have no conflict of interests to declare.

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